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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,231	07/17/2003	Changgeng Ruan	22124	4655

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/622,231	RUAN ET AL.	
	Examiner	Art Unit	
	James L Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-15 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-15 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

The disclosure is objected to because of the following informalities: the specification is replete with grammatical, idiomatic, and spelling errors and should be carefully revised. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

The specification is objected to and claims 1-14 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are: (1) known and readily available to the public; (2) reproducible from the written description; or, (3) deposited in compliance with the criteria set forth in 37 CFR §§ 1.801-1.809.

It is unclear if cell lines which produce antibodies having the exact chemical identity and properties of the antibodies listed in original claims 1 and 2 are known and publicly available, or can be reproducibly isolated without undue experimentation. Accordingly, filing of evidence of the reproducible production of the cell lines and antibodies necessary to practice the instant invention or filing of evidence of deposit is required. Without a publicly available deposit of the above cell lines, one of skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: the claimed cell line; the cell lines which produce the chemically and functionally distinct antibodies claimed; and/or, the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event. For example, very different V_H chains can combine with the same V_L chain to produce antibody binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_L sequences to produce antibodies with very similar properties. These observations indicate that divergent variable region sequences, both in and out of complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Therefore, it would require undue experimentation to reproduce the claimed monoclonal antibody species chemically as produced by the hybridomas as listed in original claims 1 and 2. A suitable deposit of the hybridomas would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See the criteria set forth in 37 CFR §§ 1.801-1.809.

If the deposits are made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the

Budapest Treaty, that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent and that the biological materials will be replaced should they ever become non-viable, would satisfy the deposit requirement made herein.

If the deposits have not been made under the Budapest Treaty, then in order to certify that the deposits meet the criteria set forth in 37 CFR §§ 1.801-1.809, applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposits will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;
(d) the deposits were viable at the time of deposit; and,
(e) the deposits will be replaced if they should ever become non-viable.

Applicant is also reminded that information regarding the deposits, such as the name and address of the depository, in addition to the accession numbers of the deposits and the date(s) of the deposits, **must** be added to the specification by means of filing an amendment as required by 37 CFR §1.809(d).

Claims 1-4 and 10-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the antibodies produced by the hybridomas R813, Y262, Y321, or Y474 (if deposited in compliance with the deposit rules, see above), does not reasonably provide enablement for all of the antibodies as listed in original claims 1 and 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicant

desires and claims antibodies which inhibit platelet aggregation functions. However, applicant teaches that of the disclosed antibodies only antibodies produced by the hybridomas R813, Y262, Y321, or Y474 had this function (see ¶ bridging pages 4 and 5). Absent further written description and guidance from applicant, one would not be assured of the ability to make and use the invention as disclosed and/or claimed with antibodies other than those produced by the hybridomas R813, Y262, Y321, or Y474.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 3, and 5, "the platelet GPIIIa" lacks antecedent basis.

In claims 2, 4 and 6, "the platelet GPIIb-IIIa complex" lacks antecedent basis.

In claims 3 and 4, the relationship of an antibody produced by immunization to the previously claimed monoclonal antibody is not clear.

In claims 5 and 6, "claim...is produced" is not clear.

In claims 7-9, "the receptor function of GPIIb-IIIa complex" lacks antecedent basis and is not clear as to what is encompassed.

In claims 10-12, "the platelet GPIIIa or platelet GPIIb-IIIa complex" lacks antecedent basis.

Claims 13 and 14 are vague in the absence of recitation of deposit accession numbers to clearly identify the antibodies/hybridomas because, absent the recitation of deposit accession numbers, it is not clear what structure and properties are encompassed by the named antibodies.

In claim 15, "the...fragment" lacks antecedent basis. Method claims should recite positive, active steps, e.g. "using" is not a proper method step.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10 and 15 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Coller (US Pat. No. 5,387,413).

Coller discloses the 7E3 monoclonal antibody and antigen-binding fragments thereof, specific for the GPIIb-IIIa complex, which was elicited by immunizing BALB/c mice with human platelets. The antibody inhibits platelet aggregation and was used in a pharmaceutical composition at an effective dose to perform this function.

Claim 10 is rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Coller et al. (US Pat. No. 5,770,198).

Coller et al. disclose the humanized 7E3 monoclonal antibody, specific for the GPIIb-IIIa complex. The antibody inhibits platelet aggregation and was used in a pharmaceutical composition at an effective dose to perform this function.

Claim 10 is rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Co et al. (US Pat. No. 5,777,085).

Co et al. disclose the humanized C4G1 monoclonal antibody, specific for the GPIIb-IIIa complex. The antibody inhibits platelet aggregation and was used in a pharmaceutical composition at an effective dose to perform this function. The reference also discloses the 10E5, AP-2, and 7E3 monoclonal antibodies specific for the GPIIb-IIIa complex and which inhibit platelet aggregation.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 2, 4, 6, 7, 9, and 12 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over either of Coller (US Pat. No. 5,387,413) or Coller et al. (US Pat. No. 5,770,198).

As set forth above, either of Coller or Coller et al. teach the 7E3 monoclonal antibody specific for the GPIIb-IIIa complex and hybridoma producing same which appears to have properties consistent with at least those of the monoclonal antibodies and hybridomas named Y262 or Y321. If not, it would have been obvious to have elicited additional antibodies with the properties of the 7E3 antibody, produced by a hybridoma, guided by the disclosures of the references. Further, the Patent and Trademark Office does not have the facilities and resources to provide the *factual* evidence needed in order to establish that there is a difference, in the first place, between the reagents of the prior art and those instantly disclosed and, that if there is such a difference, that such a difference would have been considered unexpected, i.e. unobvious, by one of ordinary skill in the art. The burden is upon applicant to present such factual evidence. See e.g. In re Best (195 USPQ 430 (CCPA 1977)) or Ex parte Phillips (28 USPQ2d 1302 (BPAI 1993)).

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Claims 1, 3, 5, 7, 8, and 11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Coller et al. (US Pat. No. 5,770,198) and Coller (US Pat. No. 5,387,413).

In addition to the teachings of the references as set forth previously, Coller et al. teach that monoclonal antibodies specific for either the GPIIb or GPIIIa components of the receptor complex could be used to inhibit platelet aggregation function of this receptor (see e.g. cols. 1 and 3).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have elicited, guided by the disclosure of Coller, and used monoclonal antibodies specific for either the GPIIb or GPIIIa components of the GPIIb-IIIa receptor complex in Coller or Coller et al. in view of the direct suggestion in the reference of Coller et al. to do so. Further, the Patent and Trademark Office does not have the facilities and resources to provide the *factual* evidence needed in order to establish that there is a difference, in the first place, between the reagents of the prior art and those instantly disclosed and, that if there is such a difference, that such a difference would have been considered unexpected, i.e. unobvious, by one of ordinary skill in the art. The burden is upon applicant to present such factual evidence. See e.g. In re Best (195 USPQ 430 (CCPA 1977)) or Ex parte Phillips (28 USPQ2d 1302 (BPAI 1993)).

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone numbers for official facsimile transmitted communications to TC 1600, Group 1640, are (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

James L. Grun, Ph.D.
March 22, 2004

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641